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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,000	05/03/2002	Tiina Nakari-Setala	0365-0529P	4534
2292 7590 02/09/2007 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER MONDESI, ROBERT B	
			ART UNIT	PAPER NUMBER
			1652	
SHORTENED STATUTORY PERIOD OF RESPONSE		NOTIFICATION DATE	DELIVERY MODE	
3 MONTHS		02/09/2007	ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/09/2007.

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mailroom@bskb.com

Office Action Summary	Application No. 10/050,000	Applicant(s) NAKARI-SETALA ET AL.	
	Examiner Robert B. Mondesi	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-34 is/are pending in the application.
- 4a) Of the above claim(s) 10-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-9 and 32-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 27, 2006 has been entered.

Status of the Claims

Claim 4 has been canceled. **Claims 33-34** have been added. **Claims 10-31** have been withdrawn. **Claims 1-3, 5-9 and 32-34** are currently pending and under examination.

Restriction requirement

This application contains **claims 10-31** drawn to an invention nonelected with traverse in Paper filed August 17, 2005. A complete reply to the final rejection mailed May 26, 2006 should have included cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn due to applicants' response in amendment filed November 27, 2006.

New Objection(s) and Rejection(s)

Specification

The disclosure is objected to because of the following informalities: In the specification on page 1, lines 6, 7 and 10 applicants have referred to the preamble of **claims 1, 12 and 34**, respectively; applicants are advised to remove such language and actually rewrite the stated phrase that is in the preamble. The main reason behind this request is to eliminate confusion should a particular claim be canceled. Of important note is also the fact that when the application was originally filed there was no **claim 34**; however presently **claim 34** has been added as a new claim and it is a depended claim without a preamble of its own.

This application contains sequence disclosures at page 13, line 13 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)((1) and (a)(2). However, this application fails to comply with one or more of the requirements of 37 C.F.R. § 1.821 through 1.825 for one or more of the reasons set forth on the attached form "Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequences And/Or Amino Acid Sequence Disclosures". Wherein attention is directed to paragraph(s) §1.82 (c) and (e). Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5-9 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific hydrophobin polypeptides, HFBI and HFBII expressed in a *Tricoderma* culture does not reasonably provide enablement for all polypeptides that are amphipathic or hydrophobic that are expressed in any fungal culture. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir.1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the

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claims, (2) the nature of the invention, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the relative skill of those in the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In *Wands*, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (*Wands*, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of *Wands* factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1-2 .Breadth of the claims and the nature of the invention.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method for decreasing the foam formation during cultivation of a fungal production host, characterized in that the process comprises the steps of genetically modifying the fungal production host in such a way that the fungal production host does not produce an essential amount of at least on the proteins, polypeptides, or peptides associated with foam formation during cultivation, said proteins, polypeptides or peptides being amphipathic or hydrophobic proteins, polypeptides or peptides, not including lipopeptides or lipoproteins; and cultivating the fungal production host under suitable conditions.

3-4. The state of prior art and the level of predictability in the art.

Nakari-Setälä et al., 1996 teach that hydrophobins are proposed to have multiple functions, some of them unknown, and their expression is regulated by a complex and diverse array of environmental conditions. For these reasons they can only be related only by structural and biochemical features.

Nakari-Setälä et al. teach further that they have characterized a new member of class II type hydrophobins, the HFBI hydrophobin of *T. reesei*. This class of hydrophobins previously contained only two other members, cryparin and cerato-ulmin which their biological roles have not been determined. However, there is some evidence that cerato-ulmin might have a role in pathogenesis.

Nakari-Setälä et al. also teach that **as is the case with many other hydrophobins, the role of HFBI in the fungus remains unknown.** One possibility is

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that this vegetative hydrophobin mediates attachment of the fungus to surfaces, as shown for class I hydrophobin Sc3p.

5. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

6-7. The amount of guidance present and the existence of working examples.

The applicant has not provided sufficient guidance for the broad method of decreasing the foam formation during cultivation of a fungal production host, characterized in that the process comprises the steps of genetically modifying the fungal production host in such a way that the fungal production host does not produce an essential amount of at least one of the proteins, polypeptides, or peptides associated with foam formation during cultivation, said proteins, polypeptides or peptides being amphipathic or hydrophobic proteins, polypeptides or peptides, not including lipopeptides or lipoproteins; and cultivating the fungal production host under suitable conditions.

However the applicants have shown some guidance and have provided some examples as far as the specific hydrophobins HFBI and HFBII of *Trichoderma* is concerned, see specification pages 17-33 and examples 1-10.

8. The quantity of experimentation necessary.

The amount of experimentation that is required is undue: while mutating the *hfb-I* and *hfb-II* genes in order to create a loss of function for the HFBI and HFBII proteins which could lead to the possible reduction of foam in a fungal culture of *Trichoderma*

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might be routine, a method of decreasing the foam formation during cultivation of a fungal production host, characterized in that the process comprises the steps of genetically modifying the fungal production host in such a way that the fungal production host does not produce an essential amount of at least one of the proteins, polypeptides, or peptides associated with foam formation during cultivation, said proteins, polypeptides or peptides being amphipathic or hydrophobic proteins, polypeptides or peptides, not including lipopeptides or lipoproteins; and cultivating the fungal production host under suitable conditions is not routine and requires more experimentation. Therefore, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

It must be noted that the issue in this case is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants' make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

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Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding an acceptable number of different fungal cultures containing an acceptable number of different amphipathic and hydrophobic polypeptides.

Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to test all the different type of different fungal cultures containing a variety of different amphipathic and hydrophobic polypeptides encompassed by the claimed invention would constitute undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Claims 1-3, 5-9 and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claim 1** applicants have cited the phrase "an essential amount"; however nowhere in the claims or the specification of the instant application have the applicants stated, qualitatively or quantitatively, as to what is meant by "an essential amount".

Claims 2-3, 5-9 and 32-34 are dependent claims that do not remedy the deficiencies of the independent claim that they are dependent therefrom.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-9 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/22598 (cited in IDS filed 2/20/2002) in view of Nakari-Setälä et al., 1997 (cited in the IDS filed 10/22/2003).

WO 98/22598 teaches a method of reducing foam formation when cultivating a fungal production wherein the gene encoding a protein associated with foam production has been genetically modified (page 5, lines 4-7; Example 12, pages 32-33).

WO 98/22598 does not teach that the protein associated with foam production is the hydrophobin HFBI or HFBII.

Nakari-Setala et al. teach that the expression of the hydrophobin proteins HFBI or HFBII have a role in causing technical problems encountered in fermentor cultivations, such as over-foaming (page 421, column 1, paragraph 4, lines 1-7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to inactivate HFBI or HFBII by mutating their related genes for the advantages of reducing foam production in a fermentation process of the fungus *Trichoderma* as taught by WO 98/22598 and Nakari-Setala, see Nakari-Setala et al. at (page 421, column 1, paragraph 4, lines 1-7) and WO 98/22598 (page 5, lines 4-7; Example 12, pages 32-33).

Conclusion

No claims are allowed

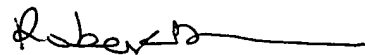
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B. Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert B Mondesi
Examiner
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1-25-2007